

CLAIMS

What we claim is:

1. A double stranded short interfering nucleic acid (siNA) molecule that comprises a first nucleotide sequence complementary to a target RNA sequence or a portion thereof, and a second sequence having complementarity to said first sequence, wherein said second sequence is chemically modified in a manner that said second sequence can no longer act as a guide sequence for mediating RNA interference.
2. The siNA molecule of claim 1, wherein said second sequence does not have a terminal 5'-hydroxyl (5'-OH) or 5'-phosphate group.
3. The siNA molecule of claim 1, wherein said second sequence comprises a terminal cap moiety at the 5'-end of said second sequence.
4. The siNA molecule of claim 1, wherein said second sequence comprises a terminal cap moiety at the 5'-end and 3'-end of said second sequence.
5. The siNA molecule of claim 3, wherein said terminal cap moiety is an inverted deoxyabasic moiety.
6. The siNA molecule of claim 4, wherein said terminal cap moiety is an inverted deoxyabasic moiety.
7. The siNA molecule of claim 1, wherein said siNA molecule comprises no ribonucleotides.
8. The siNA molecule of claim 1, wherein said siNA molecule comprises ribonucleotides.
9. The siNA molecule of claim 1, wherein said first sequence and said second sequence each comprise about 19 to about 23 nucleotides, and wherein each said sequence comprises at least about 19 nucleotides that are complementary to the nucleotides of the other strand.
10. The siNA molecule of claim 1, wherein any pyrimidine nucleotides in said second sequence are 2'-O-methyl pyrimidine nucleotides.
11. The siNA molecule of claim 1, wherein any purine nucleotides in said second sequence are 2'-deoxy purine nucleotides.

12. The siNA molecule of claim 1, wherein any pyrimidine nucleotides in said second sequence are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
13. The siNA molecule of claim 1, wherein any pyrimidine nucleotides in said first sequence are 2'-deoxy-2'-fluoro pyrimidine nucleotides
14. The siNA molecule of claim 1, wherein any purine nucleotides in said first sequence are 2'-O-methyl purine nucleotides.
15. The siNA molecule of claim 1, wherein any purine nucleotides in said first sequence comprise 2'-deoxy- purine nucleotides.
16. The siNA molecule of claim 1, wherein said first sequence comprises a phosphorothioate internucleotide linkage at the 3' end of said first sequence.
17. A pharmaceutical composition comprising the siNA molecule of claim 1 in an acceptable carrier or diluent.